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U.S. Patent Office
Art Unit 1623

July 25, 2003

Application # 09/939,385
Applicant Scott Levine

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Dear Mr. Mc Intosh:

1. Enclosed please find 5 pages that offer a Method claim and some brief substantiation of these claims.

2. 4 pages copied from the National Cholesterol Education Program Adult Treatment Program Guidelines issued by the National Institutes of Health, Heart, Lung, and Blood. Labeled pages 39-42 provided as a quick reference.

Applicant thanks examiner for his time and assistance. Applicant can be best reached at 407-296-4397.

Total Fax is 10 pages including cover.

Sincerely

Scott Levine MD

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Dear Mr. Mc Intosh:

As per previous phone conversations applicant elects **COMPOSITION** claims 24-36 and elects a method claim based on phone conversation and further discussed below.

Applicant respectfully submits a written METHOD claim for the above numbered application. Applicant respectfully submits this claim for your approval and provides some research to substantiate the Metabolic Syndrome and the Lipid claim. Applicant much appreciates the time already taken on his application and seeks to help minimize examiner's research time.

37. A method of improving the health of a mammal comprising orally administering a nutritional supplement containing at least 7 grams of fiber per serving comprising a mixture of guar, oat, and psyllium fibers plus at least one flavoring agent to a mammal at least one time daily

whereby consumption results in at least one health benefit including reducing the risk of developing and aiding in the treatment of overweight, obesity, insulin resistance, glucose intolerance, diabetes, cardiovascular disease, metabolic syndrome, abnormal serum cholesterol, lipids, lipoproteins, and triglycerides.

38. The method according to claim 37, in which at least one edible liquid selected from the group of liquids consisting of zero calorie and calorie containing liquids is admixed to said nutritional supplement of claim 37 in sufficient quantity to create at least an 8 ounce beverage selected from the group consisting of zero calorie and calorie containing beverages.

39. The method according to claim 37, further comprising:

(a) admixing at least one ingredient to form an edible food product selected from the group of solid and semisolid food products consisting of puddings, snack bars, wafers, and dog bones which is consumed at least one time daily, and

(b) said edible food product to be accompanied by consumption of sufficient quantity of at least one edible liquid selected from the group of liquids consisting of zero calorie and calorie containing liquids to further hydrate the consumed fiber.

40. The method according to claim 37, further including admixing at least one edible fiber selected from the group consisting of soluble, partially soluble, and insoluble fibers.

41. The method according to claim 37, further including admixing at least one ingredient selected from the group consisting of carbohydrates, fats, proteins, antioxidants, electrolytes, vitamins, minerals, enzymes, coenzymes, plant derived compounds, synthetic orally absorbable nontoxic compounds, organoleptic agents, coloring agents, preservatives, flavoring agents, sweeteners, stimulants, and orally consumed substances that induce weight loss.

A. **Metabolic Syndrome Claim**

Applicant submits Metabolic Syndrome information (syndrome X) from the National Institutes of Health Heart, Lung, and Blood also found on NHLBI website at http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.pdf this contains the National Cholesterol Education Program Adult Treatment Program III guidelines found on pages II 39-41 and correlates with beginning page 55 on my adobe acrobat reader.

Applicant respectfully submits that it appears that the Syndrome X is an old designation for a constellation of metabolic risk factors that is now renamed **Metabolic Syndrome** as evidence applicant provides from the NHLBI website this information

Metabolic Syndrome (current designation)

"Synonyms

- Insulin resistance syndrome

- (Metabolic) Syndrome X
- Dysmetabolic syndrome
- Multiple metabolic syndrome "

Found at website
http://hin.nhlbi.nih.gov/ncep slds/atpiii/part6txt.htm

B. **Cardiovascular Disease Claim**
Fiber has been shown to reduce risk of cardiovascular disease. Information substantiating this is found at the
a) NHLBI website
http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3 rpt.pdf
V 20 and 21 correlates with page 147-8 of my adobe acrobat reader.

Under the chapter title "Adopting healthful lifestyle habits, to lower LDL cholesterol and reduce risk of CHD" (CHD is Coronary Heart disease abbreviation). Scientific evidence recognizes that viscous fiber lowers LDL cholesterol and thereby reduces risk of CHD. As evidenced in my application, my invention lowers LDL much more than the guidelines. Evidence is provided in my 132 Declaration.

b) FDA Food labeling website information that substantiates that fiber reduces risk of heart disease.
http://www.cfsan.fda.gov/~lrd/cf101-77.html

C. **Cholesterol Claim and dietary Fiber**.

Fiber has been shown to reduce risk of cardiovascular disease. Information substantiating this is found at the
a) NHLBI website
http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3 rpt.pdf
V 20 and 21 correlates with page 147-8 of my adobe acrobat reader.

b) from FDA/cspan Food Labeling Health Claims
http://www.cfsan.fda.gov/~lrd/cf101-77.html

"4) Current dietary guidance recommendations encourage decreased consumption of dietary fat, especially saturated fat and cholesterol, and increased consumption of fiber-rich foods to help lower blood LDL-cholesterol levels. Results of numerous studies have shown that fiber-containing fruits, vegetables, and grain products can help lower blood LDL-cholesterol."

Applicant respectfully hopes this has reduced examiners search time and applicant remains available to provide further information if requested.

Applicant thanks examiner for his time and assistance with this application. Please contact applicant at 407-296-4397.

Sincerely

Scott Levine MD

From National Cholesterol Education Program ATP III guidelines

option for advanced risk assessment in appropriately selected persons, provided the test is ordered by a physician who is familiar with the strengths and weaknesses of noninvasive testing. In persons with multiple risk factors, high coronary calcium scores (e.g., >75th percentile for age and sex) denotes advanced coronary atherosclerosis and provides a rationale for intensified LDL-lowering therapy. Moreover, measurement of coronary calcium is promising for older persons in whom the traditional risk factors lose some of their predictive power (Grundy et al., 1999b). For example, a high coronary calcium score could be used to tip the balance in favor of a decision to introduce LDL-lowering drugs for primary prevention in older persons.

6. Metabolic syndrome = Syndrome X=(old name)

a. Metabolic syndrome as multiple, interrelated factors that raise risk (of Coronary Artery Disease)

This syndrome has become increasingly common in the United States. It is characterized by a constellation of metabolic risk factors in one individual (Reaven 1995; Grundy 1999a; Meigs 2000). The root causes of the metabolic syndrome are overweight/obesity, physical inactivity, and genetic factors. The metabolic syndrome is closely associated with a generalized metabolic disorder called *insulin resistance*, in which tissue responsiveness to the normal action of insulin is impaired (Kolaczynski and Caro, 1998; Zimmet et al., 1999; Haffner 1999). Some individuals are genetically predisposed to insulin resistance; in these persons, acquired factors (excess body fat and physical inactivity) elicit insulin resistance and the metabolic syndrome. Most persons with insulin resistance have abdominal obesity (Despres 1993; Despres 1998; Bjorntorp 1997). The mechanistic connections between insulin resistance and metabolic risk factors are not fully understood and appear to be complex. Various risk factors have been included in the metabolic syndrome; the following list contains those factors that are generally accepted as being characteristic of this syndrome:

- Abdominal obesity
- Atherogenic dyslipidemia
- Raised blood pressure
- Insulin resistance ± glucose intolerance
- Prothrombotic state
- Proinflammatory state

Because of the high degree of association of these risk factors in persons with the metabolic syndrome, it has proven difficult to dissect the individual contributions of each factor to CHD risk. However, there is little doubt that this syndrome taken in aggregate enhances the risk for CHD at any given LDL-cholesterol level. From a population viewpoint, the increasing prevalence of the metabolic syndrome threatens to partially reverse the reduction in CHD risk that has resulted from a decline in serum LDL cholesterol levels in the U.S. population, which has occurred over the past three decades. The metabolic syndrome and its associated risk factors have emerged as a coequal partner to cigarette smoking as contributors to premature CHD (Wilson 1998; Assmann et al., 1998b; Eckel and Krauss, 2000; National Institutes of Health 1998a,b; U.S. Department of Health and Human Services. Physical activity and health . . . 1996). In addition, the insulin resistance accompanying the metabolic syndrome is one of the underlying

causes of type 2 diabetes (Groop 1999; Cavaghan et al., 2000). For these reasons, ATP III places increased emphasis on the metabolic syndrome as a risk enhancer.

There are two general approaches to the treatment of the metabolic syndrome. The first strategy modifies root causes, overweight/obesity and physical inactivity, and their closely associated condition, insulin resistance. Weight reduction (Dengel et al., 1998; Ahmad et al., 1997; Su et al., 1995) and increased physical activity (Devlin 1992; Perseghin et al., 1996) both lower insulin resistance and indirectly mitigate the metabolic risk factors. The second approach directly treats the metabolic risk factors—atherogenic dyslipidemia, hypertension, the prothrombotic state, and underlying insulin resistance. At present, most success in clinical practice comes from pharmacological modification of the associated risk factors. However, the greatest potential for management of the syndrome lies in reversing its root causes. ATP III promotes this latter approach, which is a major new initiative for persons entering clinical cholesterol management.

Evidence statements: *The presence of the metabolic syndrome accentuates the risk accompanying elevated LDL cholesterol (C1). This increase in risk appears to be mediated through multiple risk factors—major and emerging risk factors (C1).*

Clinical trials show that modifying three major components of the metabolic syndrome—atherogenic dyslipidemia (B2), hypertension (A2, B1), and the prothrombotic state (A2, B1†)—will reduce risk for CHD.*

Recommendations: *Increased emphasis should be placed on therapeutic modification of the metabolic syndrome in persons undergoing LDL-lowering therapy. Primary management of the metabolic syndrome should be to reverse its root causes—overweight/obesity and physical inactivity. In addition, other lipid and nonlipid risk factors associated with the metabolic syndrome should be appropriately treated.*

The presence of the metabolic syndrome provides the option to intensify LDL-lowering therapy after LDL-cholesterol goals are set with the major risk factors. Primary emphasis nonetheless should be given to modifying the underlying risk factors (overweight/obesity and physical inactivity) and other risk factors associated with the metabolic syndrome.

* See JNC VI. (JNC VI 1997; Joint National Committee . . . 1997).

† See results of meta-analysis of aspirin trials.

b. Diagnosis of metabolic syndrome

There are no well-accepted criteria for the diagnosis of the metabolic syndrome. Nonetheless, many persons seen in clinical practice are readily recognized as having multiple metabolic risk factors. Most persons with the metabolic syndrome are overweight or obese; clinical studies have noted a high correlation between abdominal obesity and the risk factors characteristic of the metabolic syndrome (Bjorntorp 1997; Despres 1993; Okosun et al., 2000; Bjorntorp 1992). For example, closely associated with abdominal obesity is an elevation of serum triglycerides (Mekki et al., 1999; Bodkin et al., 1993; Julien et al., 1997). The elevation can be either borderline high (150–199 mg/dL) or high (≥200 mg/dL). A higher triglyceride level is usually accompanied by lower HDL-cholesterol concentrations (Phillips et al., 1981; Schaefer et al., 1988). HDL-

Epitome Means "Ideal example" Webster's Dictionary

cholesterol levels <40 mg/dL occur commonly in men with insulin resistance (Karhapaa et al., 1994). Further, moderate (marginal) reductions of HDL-cholesterol levels are observed commonly in women with the syndrome (Nilsson et al., 2000; Vanhala et al., 1997); thus for women, HDL cholesterol <50 mg/dL counts as one indicator in the diagnosis of the metabolic syndrome. A moderately strong association exists between insulin resistance and hypertension (Lind et al., 1995; Lender et al., 1997; Landsberg 1999). Insulin resistance also is associated with high-normal blood pressure (Dyer et al., 1999; Falkner et al., 1999).

Impaired fasting glucose (110–125 mg/dL) usually is an indicator of insulin resistance and is frequently accompanied by other metabolic risk factors (Tripathy et al., 2000; Haffner et al., 1996); measurement of fasting glucose in overweight and obese persons is a reasonable option (National Institutes of Health 1998a,b). A portion of persons with impaired fasting glucose will eventually develop type 2 diabetes (Edelstein et al., 1997; Lindahl et al., 1999), which further enhances risk for CHD. Type 2 diabetes is the epitome of the metabolic syndrome. Other components of the metabolic syndrome (insulin resistance, proinflammatory state, and prothrombotic state) cannot be identified by routine clinical evaluation. However, in the presence of abdominal obesity, they often are present. For present purposes, the metabolic syndrome is identified by the presence of three or more of the components listed in the following table.

Table II.6–1. Clinical Identification of the Metabolic Syndrome*

3 or more of these makes the diagnosis.

Risk Factor	Defining Level
Abdominal Obesity Men Women	Waist Circumference† >102 cm (>40 in) >88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol Men Women	 <40 mg/dL <50 mg/dL
Blood pressure	≥130/85 mmHg
Fasting glucose	110–125 mg/dl

* The ATP III panel did not find adequate evidence to recommend routine measurement of insulin resistance (e.g., plasma insulin), proinflammatory state (e.g., high-sensitivity C-reactive protein), or prothrombotic state (e.g., fibrinogen or PAI-1) in the diagnosis of the metabolic syndrome.

† Some male persons can develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g., 94–102 cm (37–39 in). Such persons may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.

c. Metabolic syndrome as a target of therapy

In persons entering clinical management of elevated LDL cholesterol, the full benefit of risk reduction will be lost if the metabolic syndrome is ignored. To achieve maximal benefit from modification of multiple metabolic risk factors, the underlying insulin resistant state must become a target of therapy. The safest, most effective, and preferred means to reduce insulin resistance is weight reduction in overweight and obese persons and increased physical activity. Both weight control (Dengel et al., 1998; Ahmad et al., 1997; Su et al., 1995) and exercise

(Devlin 1992; Perseghin et al., 1996; Hu et al., 2001; Farrell et al., 1998) reduce insulin resistance and favorably modify the metabolic risk factors, ATP III thus places increased emphasis on the metabolic syndrome and on its favorable modification through changes in life habits.

Drug treatment of several of the individual risk factors of the metabolic syndrome will reduce risk for CHD. The strong trend for benefit of drug treatment of atherogenic dyslipidemia is discussed in Section II.3. Risk reductions by lowering blood pressure with antihypertensive drugs (JNC VI 1997; Joint National Committee . . . 1997) and treating the prothrombotic state with aspirin (Henneken et al., 1997) are well established. However, lowering serum glucose with drugs has not yet been documented to reduce risk for CHD. Although drugs are available to reduce insulin resistance, there is no clear evidence yet that they will reduce risk for CHD in persons with the metabolic syndrome.

END of Metabolic Syndrome

7. Primary prevention: persons without established CHD

a. Scope of primary prevention

Primary prevention aims to prevent new onset CHD. If prevention is delayed until advanced coronary atherosclerosis has developed, the U.S. public will continue to suffer from a heavy burden of CHD. The essential approach to primary prevention is to reduce risk factors for CHD. Waiting until a diagnosis of CHD is made before beginning risk factor reduction will miss the opportunity to prevent CHD in people whose first presentation is sudden cardiac death or disability (deVreede-Swagemakers et al., 1997; Kannel 1985b; Muller et al., 1997; American Heart Association 1998). One-third of people who experience a myocardial infarction will die within 24 hours and many survivors will have serious morbidity including congestive heart failure, angina, arrhythmias, and an increased risk of sudden death (American Heart Association 1998). One-third of all new cardiovascular events occurs in individuals under age 65 (AHA Heart Facts, 1999). These observations argue strongly for primary prevention of CHD.

Elevations of serum LDL cholesterol contribute importantly to the high prevalence of CHD in the United States. International studies find that CHD is uncommon in cultures with low levels of serum cholesterol even when the prevalence of hypertension and cigarette smoking is relatively high (Keys 1980; Grundy et al., 1990; Tunstall-Pedoe et al., 1994). Migration studies reveal that persons who emigrate from low-risk to high-risk cultures show a rise in LDL-cholesterol levels and assume the risk of the new culture (Marmot et al., 1975). Mass elevations of serum LDL cholesterol result from the habitual diet in the United States, particularly diets high in saturated fats and cholesterol (Keys et al., 1980; Blackburn 1990; Krauss et al., 1996; 2000; U.S. Department of Agriculture . . . 2000). When these diets are combined with a relatively heavy burden of other CHD risk factors, a high prevalence of premature CHD results.

b. Clinical strategy in primary prevention effort

NCEP supports two complementary approaches to primary prevention: (1) population strategies and (2) clinical strategies (National Cholesterol Education Program 1990; Report of the Expert Panel on Population Strategies . . . 1991). NCEP encourages dietary and other behavioral